BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

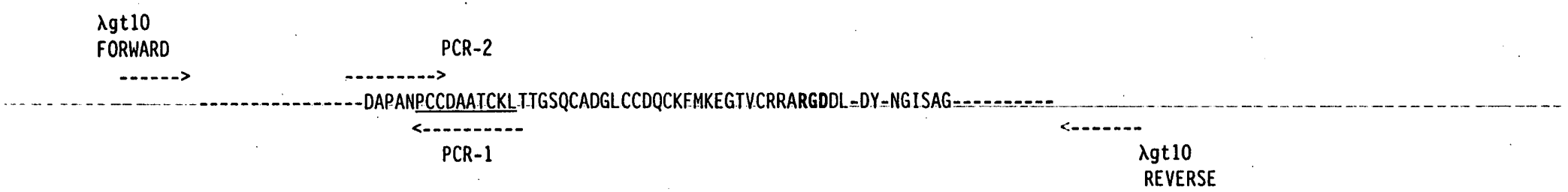
As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

FIG. 1

A. Comparison of disintegrin amino acid sequences:

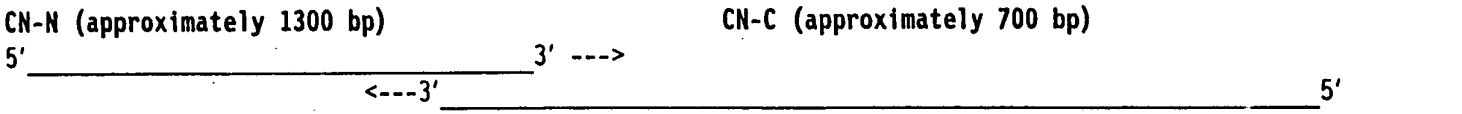
```
Contortrostatin            DAPANPCCDAATCKLTTGSQCADGLCCDQCKFMKEGTVC-RARGDDL-DY-NGISAG----
Applagin          EAGEECDCGSPENPCCDAATCKLRPGAQCAEGLCCDQCKFMKEGTVC-RARGDDVNDYCNGISAGCPRNPFH
Trigramin         EAGEDCDCGSPANPCCDAATCKLIPGAQCGEGLCCDQCSFIEEGTVCRIARGDDLDDYCNGRSAGCPRNPFH
Albolabrin        EAGEDCDCGSPANPCCDAATCKLLPGAQCGEGLCCDQCSFMKKGTICRRARGDDLDDYCNGISAGCPRNPLHA
Elegantin         EAGEECDCGSPENPCCDAATCKLRPGAQCADGLCCDQCRFKKKRTICRRARGDNPDDRCTGQSADCPRNGLYS
Kistrin             GKECDCSSPENPCCDAATCKLRPGAQCGEGLCCEQCKFDRAGKICRIPRGDMPDDRCTGQSADCPRYH
```

B. Design of PCR primers:

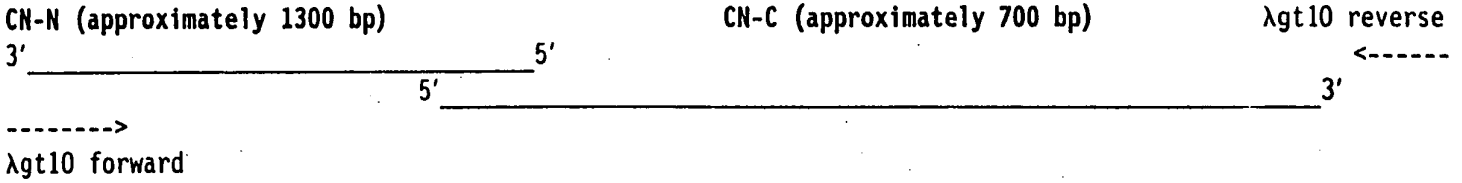


C. Overlapping extension of PCR fragments:

(a) self-extendible molecule:



(b) non-self-extendible molecule:



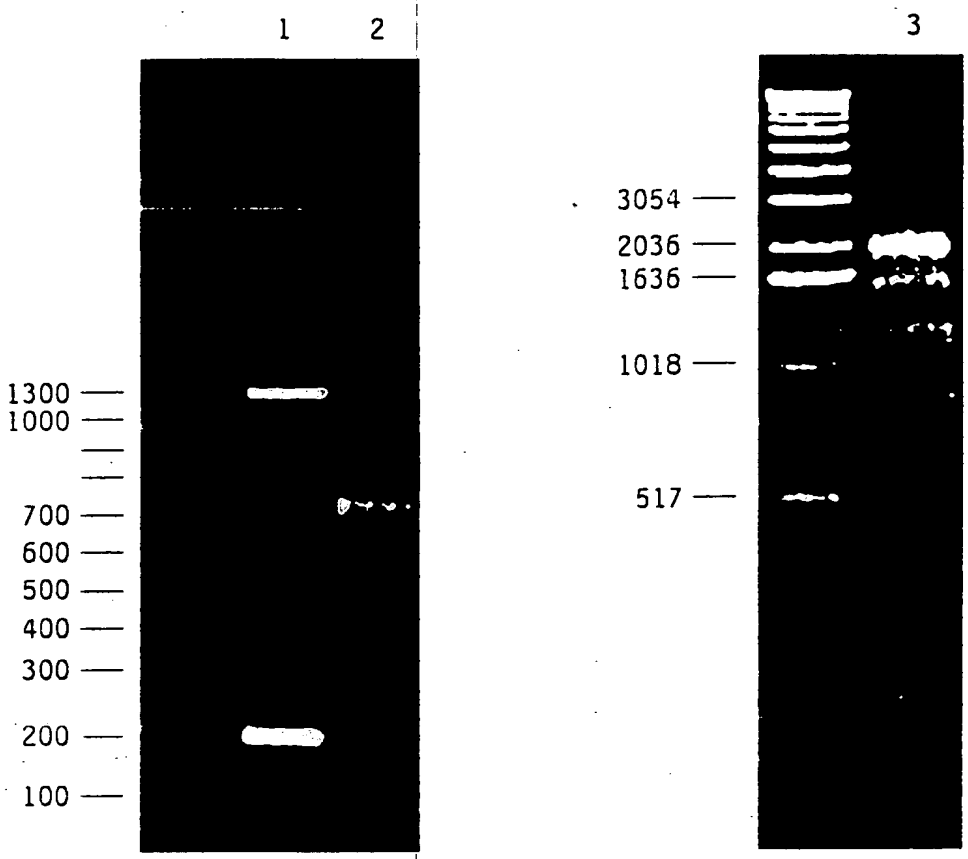

1
2
3
1300
1000
700
600
500
400
300
200
100
3054
2036
1636
1018
517

FIG. 2

FIG. 3A

```
                11          20          29          38          47          56
5' GA ATT CGG GGT CAA TAG AGG AAG AGC TCA AGT TGG CTT GAA AGC AGG AAG AGA TTG

            65          74          83          92          101         110
    CCT GTC TTC CAG CCA AAT CCA GCC GCC AAA ATG ATC CAG GTT CTC TTG GTG ACT
                                        --- --- --- --- --- --- --- ---
[1]                                      M   I   Q   V   L   L   V   T [8]

            119         128         137         146         155         164
    CTA TGC TTA GCA GCT TTT CCT TAT CAA GGG AGC TCT ATA ATC CTG GAA TCT GGG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[9]  L   C   L   A   A   F   P   Y   Q   G   S   S   I   I   L   E   S   G [26]

            173         182         191         200         209         218
    AAT GTT AAT GAT TAT GAA GTA CTG TAT CCA CAA AAA GTC ACT GCA TTG CCC AAA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[27] N   V   N   D   Y   E   V   L   Y   P   Q   K   V   T   A   L   P   K [44]

            227         236         245         254         263         272
    GGA GCA GTT CAG CCA AAG TAT GAA GAC ACC ATG CAA TAT GAA TTT AAA GTG AAT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[45] G   A   V   Q   P   K   Y   E   D   T   M   Q   Y   E   F   K   V   N [62]

            281         290         299         308         317         326
    GGA GAG CCA GTG GTC CTT CAC CTG GAA AAA AAT AAA GGA CTT TTT TCA AAA GAT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[63] G   E   P   V   V   L   H   L   E   K   N   K   G   L   F   S   K   D [80]

            335         344         353         362         371         380
    TAC AGC GAG ACT CAT TAT TCC TCT GAT GGC AGA AAA ATT ACA ACA AAC CCT CCG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[81] Y   S   E   T   H   Y   S   S   D   G   R   K   I   T   T   N   P   P [98]

            389         398         407         416         425         434
    GTT GAG GAT CAC TGC TAT TAT CAT GGA CGC ATC CAG AAT GAT GCT GAC TCA ACT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[99] V   E   D   H   C   Y   Y   H   G   R   I   Q   N   D   A   D   S   T [116]

            443         452         461         470         479         488
    GCA AGC ATC AGT GCA TGC AAC GGT TTG AAA GGA CAT TTC AAG CTT CAA GGG GAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[117]A   S   I   S   A   C   N   G   L   K   G   H   F   K   L   Q   G   E [134]

            497         506         515         524         533         542
    ACG TAC CTT ATT GAA CCC TTG AAG CTT TCC GAC AGT GAA GCC CAT GCA GTC TAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[135]T   Y   L   I   E   P   L   K   L   S   D   S   E   A   H   A   V   Y [152]

            551         560         569         578         587         596
    AAA TAT GAA AAC GTA GAA AAA GAA GAT GAG GCC CCC AAA ATG TGT GGG GTA ACC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[153]K   Y   E   N   V   E   K   E   D   E   A   P   K   M   C   G   V   T [170]
```

FIG. 3B

```
          605        614        623        632        641        650
    CAG ACT AAT TGG GAA TCA GAT GAG CCC ATC AAA AAG GCC TCT CAG TTA AAT CTT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[171]Q   T   N   W   E   S   D   E   P   I   K   K   A   S   Q   L   N   L [188]

          659        668        677        686        695        704
    ACT CCT GAA CAA CAA GGA TTC CCC CAA AGA TAC ATT GAG CTT GTT GTA GTT GCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[189]T   P   E   Q   Q   G   F   P   Q   R   Y   I   E   L   V   V   V   A [206]

          713        722        731        740        749        758
    GAT CAC AGA ATG TTC ACG AAA TAC AAC GGC AAT TTA AAT ACT ATT AGA ATA TGG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[207]D   H   R   M   F   T   K   Y   N   G   N   L   N   T   I   R   I   W [224]

          767        776        785        794        803        812
    GTA CAT GAA CTT GTC AAC ACT ATG AAT GTG TTT TAC AGA CCT TTG AAT ATT CGT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[225]V   H   E   L   V   N   T   M   N   V   F   Y   R   P   L   N   I   R [242]

          821        830        839        848        857        866
    GTC TCA CTG ACT GAC CTA GAA GTT TGG TCA GAC CAA GAT TTG ATC AAC GTG CAG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[243]V   S   L   T   D   L   E   V   W   S   D   Q   D   L   I   N   V   Q [260]

          875        884        893        902        911        920
    CCA GCA GCG GCT GAT ACT TTG GAA GCA TTT GGA GAC TGG AGA GAG ACA GTC TTG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[261]P   A   A   A   D   T   L   E   A   F   G   D   W   R   E   T   V   L [278]

          929        938        947        956        965        974
    CTG AAT CGC ATA AGT CAT GAT AAT GCT CAG TTA CTC ACG GCC ATT GAG CTT GAT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[279]L   N   R   I   S   H   D   N   A   Q   L   L   T   A   I   E   L   D [296]

          983        992       1001       1010       1019       1028
    GGA GAA ACT ATA GGA TTG GCT AAC AGG GGC ACC ATG TGC GAC CCG AAG CTT TCT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[297]G   E   T   I   G   L   A   N   R   G   T   M   C   D   P   K   L   S [314]

         1037       1046       1055       1064       1073       1082
    ACA GGA ATT GTT CAG GAT CAT AGT GCA ATA AAT CTT TGG GTT GCA GTT ACA ATG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[315]T   G   I   V   Q   D   H   S   A   I   N   L   W   V   A   V   T   M [332]

         1091       1100       1109       1118       1127       1136
    GCC CAT GAG ATG GGT CAT AAT CTG GGT ATT AGT CAC GAT GGA AAT CAG TGT CAT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[333]A   H   E   M   G   H   N   L   G   I   S   H   D   G   N   Q   C   H [350]

         1145       1154       1163       1172       1181       1190
    TGC GAT GCT AAC TCA TGC ATT ATG AGT GAA GAA CTA AGA GAA CAA CTT TCC TTT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[351]C   D   A   N   S   C   I   M   S   E   E   L   R   E   Q   L   S   F [368]
```

FIG. 3C

```
          1199        1208        1217        1226        1235        1244
    GAG TTC AGC GAT TGT AGT CAG AAT CAA TAT CAG ACA TAT CTT ACT GAT CAT AAC
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[369]E   F   S   D   C   S   Q   N   Q   Y   Q   T   Y   L   T   D   H   N [386]

          1253        1262        1271        1280        1289        1298
    CCA CAA TGC ATG CTC AAT GAA CCC TTG AGA ACA GAT ATT GTT TCA ACT CCA GTT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[387]P   Q   C   M   L   N   E   P   L   R   T   D   I   V   S   T   P   V [404]

          1307        1316        1325        1334        1343        1352
    TCT GGA AAT GAA CTT TTG GAG ACG GGA GAA GAA AGT GAC TTT GAC GCT CCT GCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[405]S   G   N   E   L   L   E   T   G   E   E   S   D   F   D   A   P   A [422]

          1361        1370        1379        1388        1397        1406
    AAT CCG TGC TGC GAT GCT GCA ACA TGT AAA CTG ACA ACA GGG TCA CAG TGT GCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[423]N   P   C   C   D   A   A   T   C   K   L   T   T   G   S   Q   C   A [440]

          1415        1424        1433        1442        1451        1460
    GAT GGA CTG TGT TGT GAC CAG TGC AAA TTT ATG AAA GAA GGA ACA GTA TGC CGG
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[441]D   G   L   C   C   D   Q   C   K   F   M   K   E   G   T   V   C   R [458]

          1469        1478        1487        1496        1505        1514
    AGA GCA AGG GGT GAT GAC CTG GAT GAT TAC TGC AAT GGC ATA TCT GCT GGC TGT
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[459]R   A   R   G   D   D   L   D   D   Y   C   N   G   I   S   A   G   C [476]

          1523        1532        1541        1550        1559        1568
    CCC AGA AAT CCC TTC CAT GCC TAA CCA ACA ATG GAG ATG GAA TGG TCT GCA GCA
    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- ---
[477]P   R   N   P   F   H   A   * [483]

          1577        1586        1595        1604        1613        1622
    ACA GGC AGT GTG TTG ATC TGA ATA CAG CCT AAT AAT CAA CCT CTG GCT TCT CTC

          1631        1640        1649        1658        1667        1676
    AGA TTT GAT CAT GGA GAT CCT TCT TCC AGA AGG TTT CAC TTC CCT CAA ATC CAA

          1685        1694        1703        1712        1721        1730
    AGA GAC CCA TCT GCC TGC ATC CTA CTA GTA AAT CAC CCT TAG CTT CCA GAT GGT

          1739        1748        1757        1766        1775        1784
    ATC CAA ATT CTG TAA TAT TTC TTC TCC ATA TTT AAT CTA TTT ACC TTT TGC TGT

          1793        1802        1811        1820        1829        1838
    AAC AAA ACC TTT TTC CTG TCA CAA AGC TCC ATG GGC ATG TAC AGC TTA TCT GCT

          1847        1856        1865        1874        1883        1892
    GTC AAG AAA AAA AAT GGC CAT TTT ACC GTT TGC CAG TTA CAA AGC ACA TTT AAT

          1901        1910        1919        1928        1937        1946
    GCA ACA AGT TCT TCC TTT TGA GCT GAT GTA TTC AAA GTC AAT GCT TCC TCT CCC
```

FIG. 3D

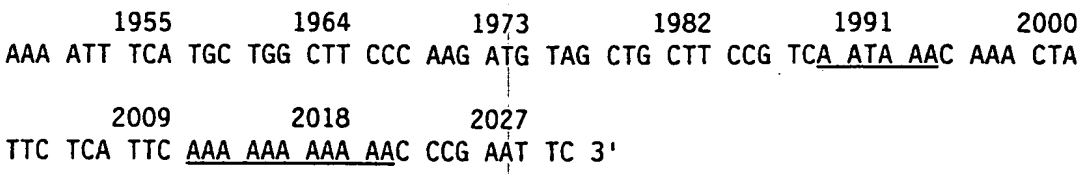

1955 1964 1973 1982 1991 2000
AAA ATT TCA TGC TGG CTT CCC AAG ATG TAG CTG CTT CCG TCA ATA AAC AAA CTA
2009 2018 2027
TTC TCA TTC AAA AAA AAA AAC CCG AAT TC 3'

FIG. 4-1

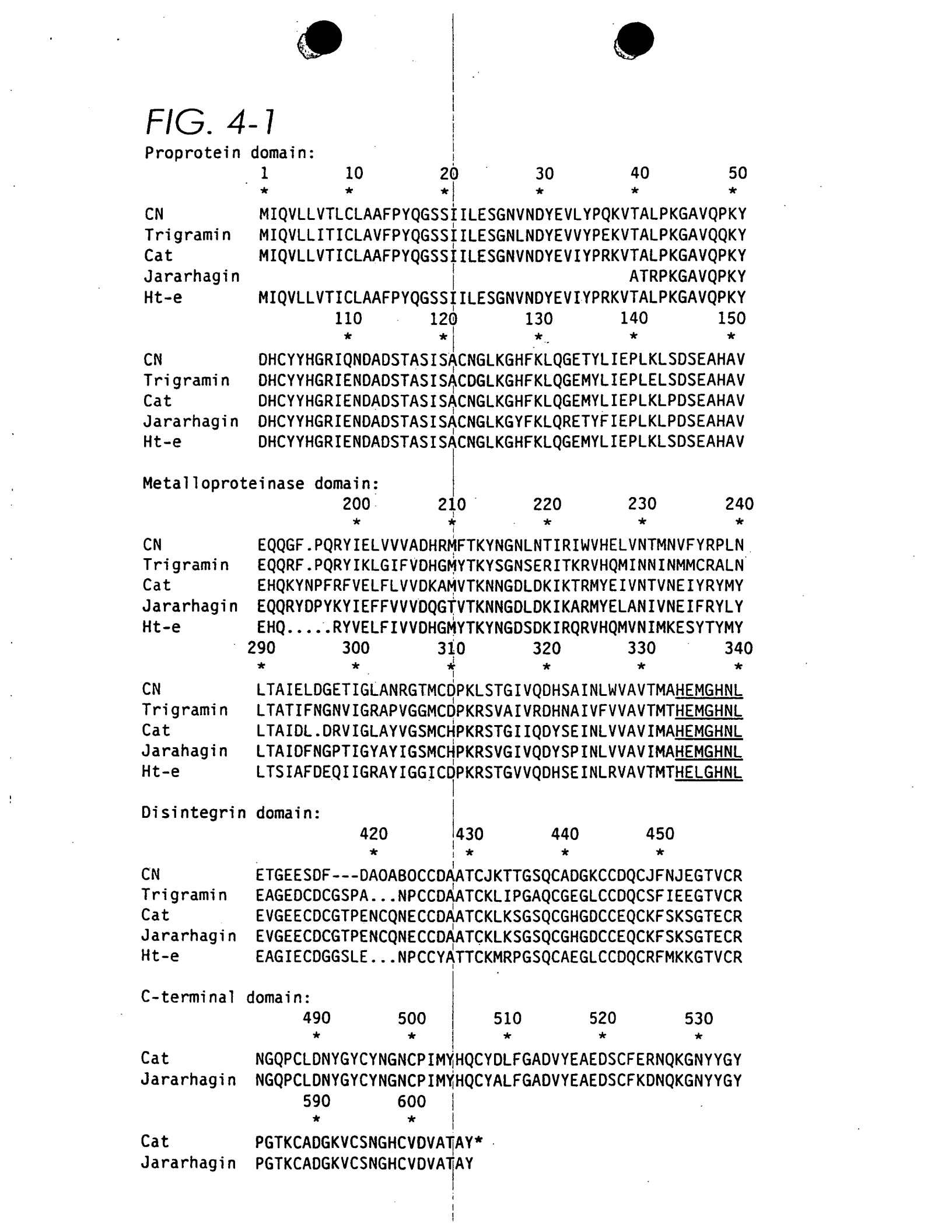

Proprotein domain:
1 10 20 30 40 50
CN MIQVLLVTLCLAAFPYQGSSIILESGNVNDYEVLYPQKVTALPKGAVQPKY
Trigramin MIQVLLITICLAVFPYQGSSIILESGNLNDYEVVYPEKVTALPKGAVQQKY
Cat MIQVLLVTICLAAFPYQGSSIILESGNVNDYEVIYPRKVTALPKGAVQPKY
Jararhagin ATRPKGAVQPKY
Ht-e MIQVLLVTICLAAFPYQGSSIILESGNVNDYEVIYPRKVTALPKGAVQPKY
110 120 130 140 150
CN DHCYYHGRIQNDADSTASISACNGLKGHFKLQGETYLIEPLKLSDSEAHAV
Trigramin DHCYYHGRIENDADSTASISACDGLKGHFKLQGEMYLIEPLELSDSEAHAV
Cat DHCYYHGRIENDADSTASISACNGLKGHFKLQGEMYLIEPLKLPDSEAHAV
Jararhagin DHCYYHGRIENDADSTASISACNGLKGYFKLQRETYFIEPLKLPDSEAHAV
Ht-e DHCYYHGRIENDADSTASISACNGLKGHFKLQGEMYLIEPLKLSDSEAHAV
Metalloproteinase domain:
200 210 220 230 240
CN EQQGF.PQRYIELVVVADHRMFTKYNGNLNTIRIWVHELVNTMNVFYRPLN
Trigramin EQQRF.PQRYIKLGIFVDHGMYTKYSGNSERITKRVHQMINNINMMCRALN
Cat EHQKYNPFRFVELFLVVDKAMVTKNNGDLDKIKTRMYEIVNTVNEIYRYMY
Jararhagin EQQRYDPYKYIEFFVVVDQGTVTKNNGDLDKIKARMYELANIVNEIFRYLY
Ht-e EHQ.....RYVELFIVVDHGMYTKYNGDSDKIRQRVHQMVNIMKESYTYMY
290 300 310 320 330 340
CN LTAIELDGETIGLANRGTMCDPKLSTGIVQDHSAINLWVAVTMAHEMGHNL
Trigramin LTATIFNGNVIGRAPVGGMCDPKRSVAIVRDHNAIVFVVAVTMTHEMGHNL
Cat LTAIDL.DRVIGLAYVGSMCHPKRSTGIIQDYSEINLVVAVIMAHEMGHNL
Jarahagin LTAIDFNGPTIGYAYIGSMCHPKRSVGIVQDYSPINLVVAVIMAHEMGHNL
Ht-e LTSIAFDEQIIGRAYIGGICDPKRSTGVVQDHSEINLRVAVTMTHELGHNL
Disintegrin domain:
420 430 440 450
CN ETGEESDF---DAOABOCCDAATCJKTTGSQCADGKCCDQCJFNJEGTVCR
Trigramin EAGEDCDCGSPA...NPCCDAATCKLIPGAQCGEGLCCDQCSFIEEGTVCR
Cat EVGEECDCGTPENCQNECCDAATCKLKSGSQCGHGDCCEQCKFSKSGTECR
Jararhagin EVGEECDCGTPENCQNECCDAATCKLKSGSQCGHGDCCEQCKFSKSGTECR
Ht-e EAGIECDGGSLE...NPCCYATTCKMRPGSQCAEGLCCDQCRFMKKGTVCR
C-terminal domain:
490 500 510 520 530
Cat NGQPCLDNYGYCYNGNCPIMYHQCYDLFGADVYEAEDSCFERNQKGNYYGY
Jararhagin NGQPCLDNYGYCYNGNCPIMYHQCYALFGADVYEAEDSCFKDNQKGNYYGY
590 600
Cat PGTKCADGKVCSNGHCVDVATAY*
Jararhagin PGTKCADGKVCSNGHCVDVATAY

FIG. 4-2

```
         60        70        80        90        100
         *         *         *         *         *
EDTMQYEFKVNGEPVVLHLEKNKGLFSKDYSETHYSSDGRKITTNPPVE
EDAMQYEFKVNGEPVVLHLEKNKGLFSEDYSEIHYSPDGREITAYPSVE
EDAMQYELKVNGEPVVLHLGKNKGLFSKDYSETHYSPDGREITTYPLVE
EDAMQYEFKVNGEPVVLHLEKNKGLFSKDYSEIHYSPDGREITTYPPVE
EDTMQYELKVNGEPVVLHLEKNKGLFSKDYSETHYSFDGRKITTNPSVE
        160       170       180       190
         *         *         *         *
YKYENVEKEDEAPKMCGVTQTNWESDEPIKKASQLNLTP
FKYENVEKEDEPPKMCGVTQ.NWESYESTKKASQLNVTP
YKYENVEKEDEALKMCGVTQ.NWESYEPIKKASQLVVTA
FKYENVEKEDEAPKMCGVTQ.NWKSYEPIKKASQLAFTA
FKLKNVEKEDEAPKMCGVTQ.NWESYEPIKKASDLNLNP


         250       260       270       280
         *         *         *         *
IRVSLTDLEVWSDQDLINVQPAAADTLEAFGD.WRETVLLNRISHDNAQL
IVTTLSVLEIWSEKDLITVQ.ASAPTTLTLFGAWRETVLLNRTSHDHAQL
IHVALVGLEIWSNEDKITVKPEAGYTLNA.FGEWRKTDLLTRKKHDNAQL
MHVALVGLEIWSNGDKITVKPDVDYTLNS.FAEWRKTDLLTRKKHDNAQL
IDILLAGIEIWSNGDLINVQPASPNTLNS.FGEWRETDLLKRKSHDNAQL
         350       360       370       380       390       400       410
          *         *         *         *         *         *         *
GISHDGNQCHCDANSCIMSEELREQLSFEFSDCSQNQYQTYLTDHNPQCMLNEPLRTDIVSTPVSGNELL
GMHHDEDKCNCN..TCIMSKVLSRQPSKYFSECSKDYYQTFLTNHNPQCILNAPLRTDTVSTPVSGNELL
GINHDSGYCSCGDYACIMRPEISPEPSTFFSNCSYFECWDFIMNHNPECILNEPLGTDIISPPVCGNELL
GIHHDTGSCSCGDYPCIMGPTISNEPSKFFSNCSYIQCWDFIMNHNPECIINEPLGTDIISPPVCGNELL
GIHHDTDSCSCGGYSCIMSPVISDEPSKYFSDCSYIQCWEFIMNQKPQCILKKPLRTDTVSTPVSGNELL


 460       470       480
  *         *         *
RARGD.DLDDYCNGISAGCPRNPFHA*
IARGD.DLDDYCNGRSAGCPRNPFHA
ASMSECDPAEHCTGQSSECPADVFHK
ASMSECDPAEHCTGQSSECPADVFHK
VSMVDRN.DDTCTGQSADCPRNGLYG*


    540       550       560       570       580
     *         *         *         *         *
CRKENGNKIPCAPEDVKCGRLYCKDNSPGQNNPCKMFYSNEDEHKGMVL
CRKENGKKIPCAPEDVKCGRLYCKDNSPGQNNPCKMFYSNDDEHKGMVL
```

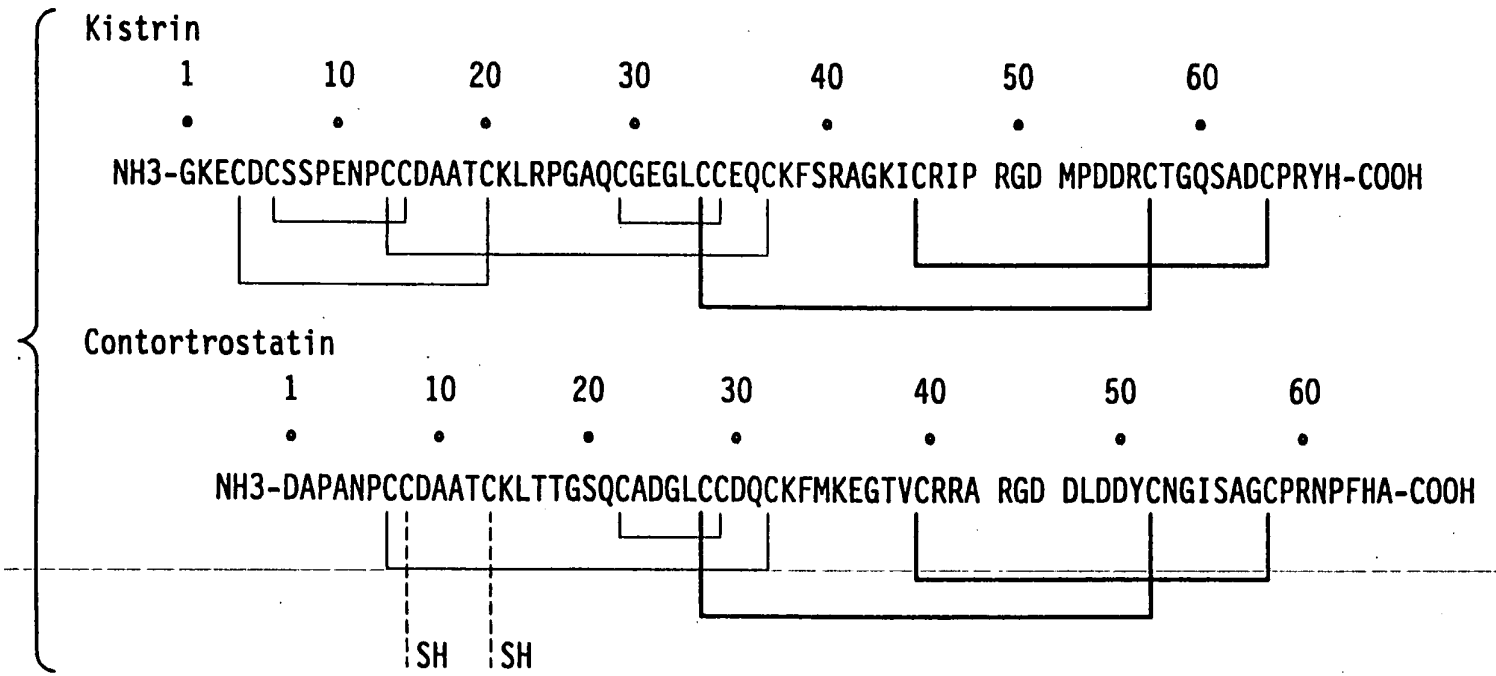

Kistrin
1
10
20
30
40
50
60
NH3-GKECDCSSPENPCCDAATCKLRPGAQCGEGLCCEQCKFSRAGKICRIP RGD MPDDRCTGQSADCPRYH-COOH
Contortrostatin
1
10
20
30
40
50
60
NH3-DAPANPCCDAATCKLTTGSQCADGLCCDQCKFMKEGTVCRRA RGD DLDDYCNGISAGCPRNPFHA-COOH
SH
SH

FIG. 5A

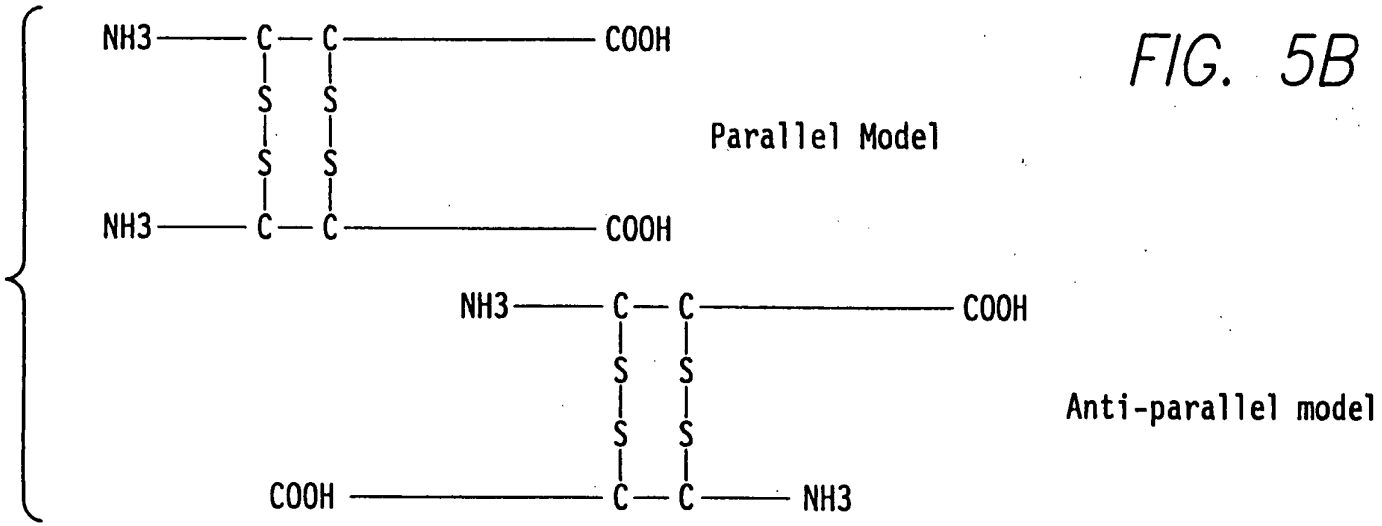

NH3
C
C
COOH
S
S
S
S
NH3
C
C
COOH
Parallel Model
NH3
C
C
COOH
S
S
S
S
COOH
C
C
NH3
Anti-parallel model

FIG. 5B

FIG. 6

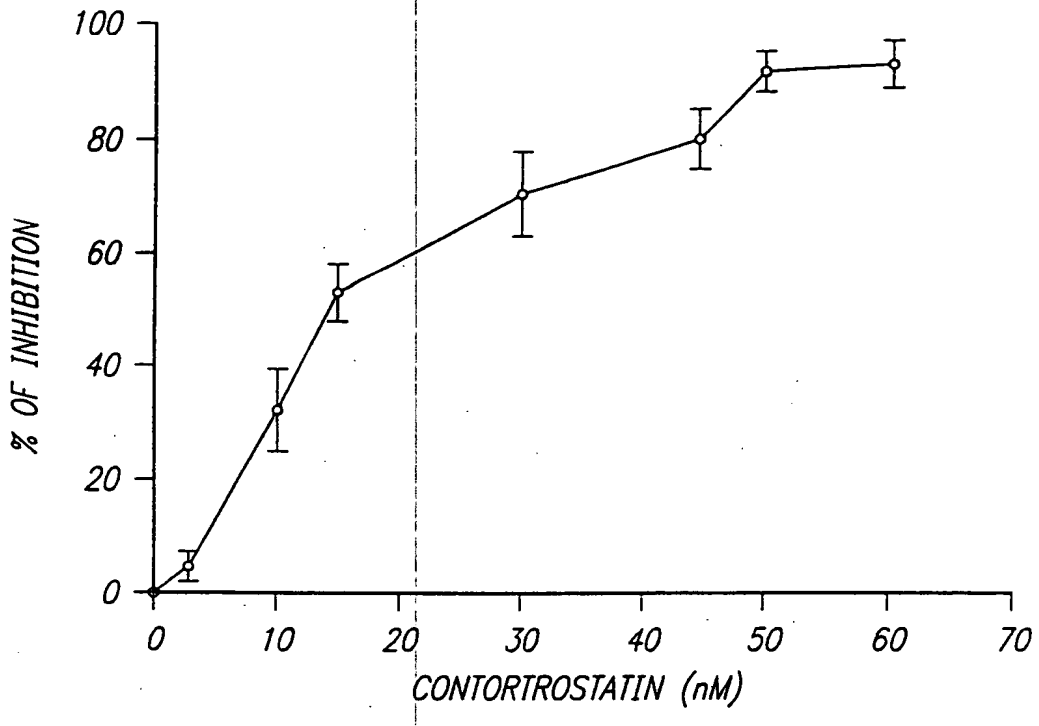

100
80
60
40
20
0
% OF INHIBITION
0
10
20
30
40
50
60
70
CONTORTROSTATIN (nM)

FIG. 7

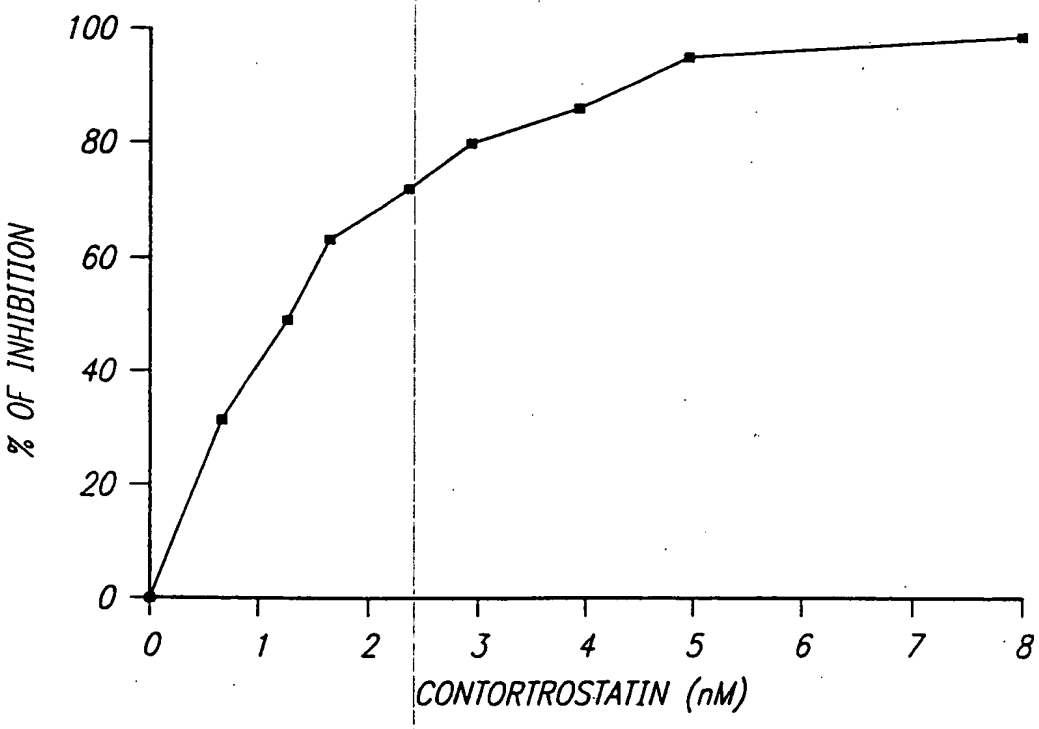

100
80
60
40
20
0
% OF INHIBITION
0
1
2
3
4
5
6
7
8
CONTORTROSTATIN (nM)

FIG. 8

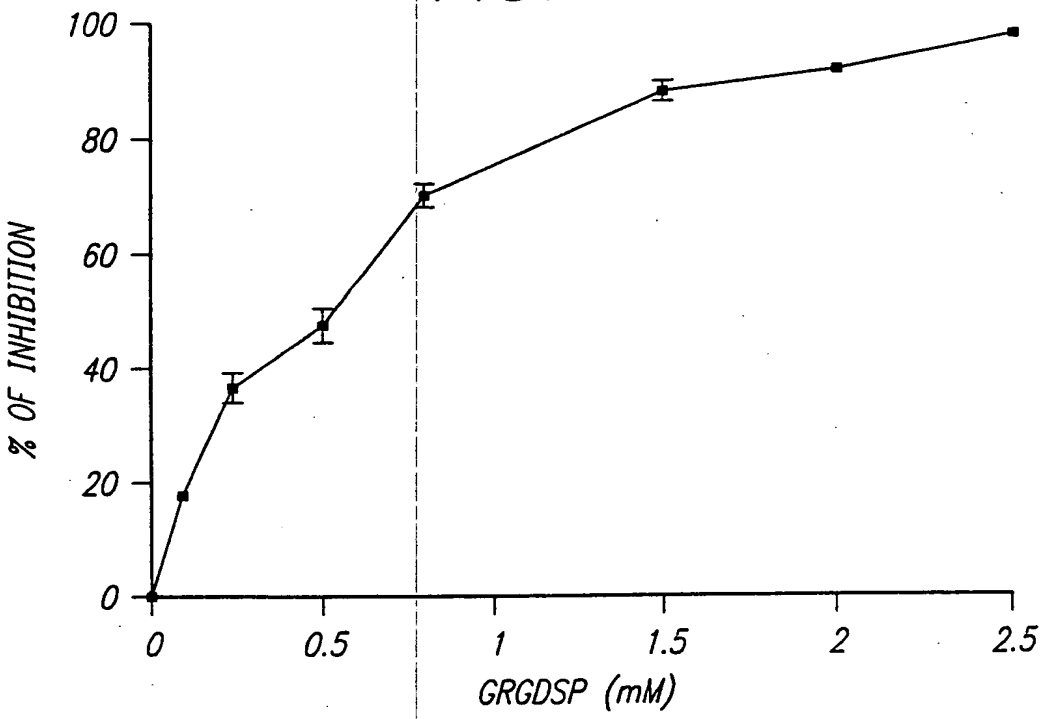
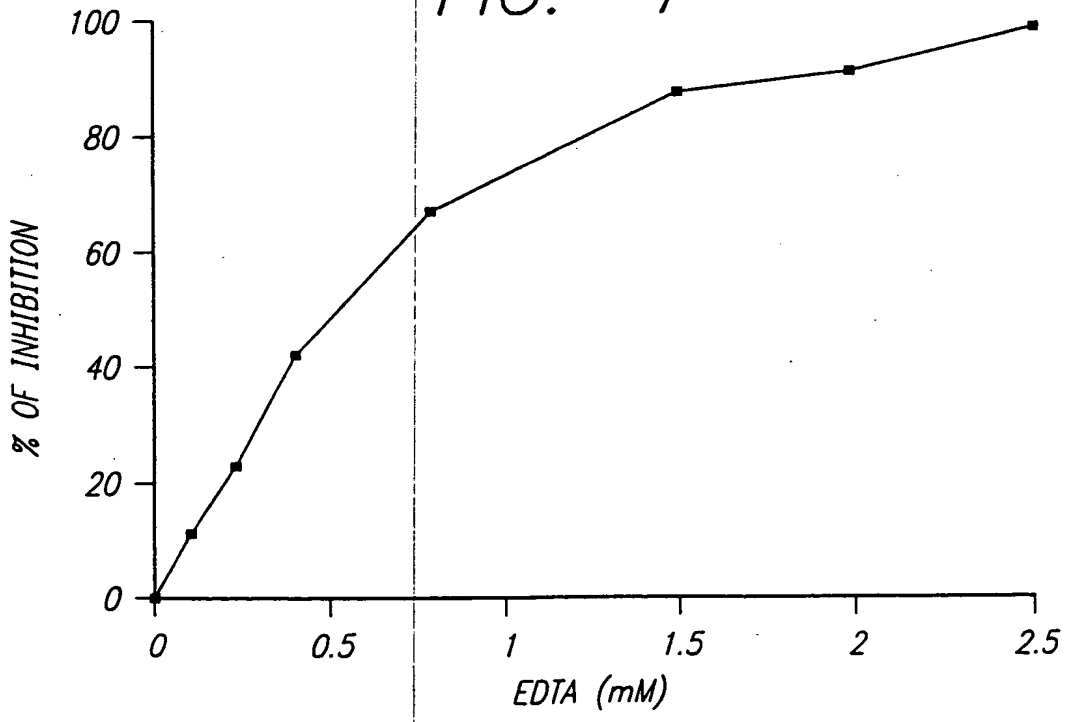
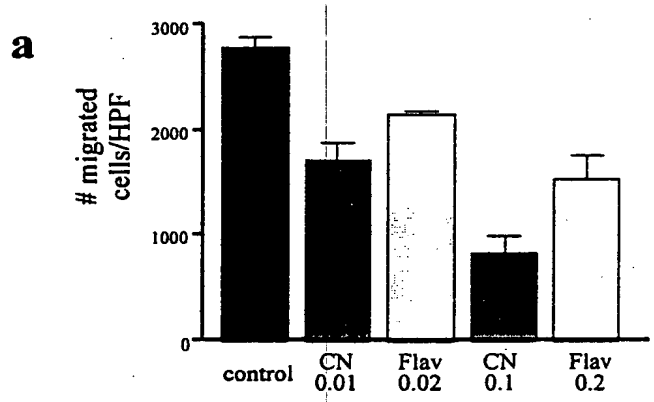

100
80
60
40
20
0
% OF INHIBITION
0
0.5
1
1.5
2
2.5
GRGDSP (mM)

FIG. 9


100
80
60
40
20
0
% OF INHIBITION
0
0.5
1
1.5
2
2.5
EDTA (mM)


a
migrated cells/HPF
3000
2000
1000
0
control
CN 0.01
Flav 0.02
CN 0.1
Flav 0.2

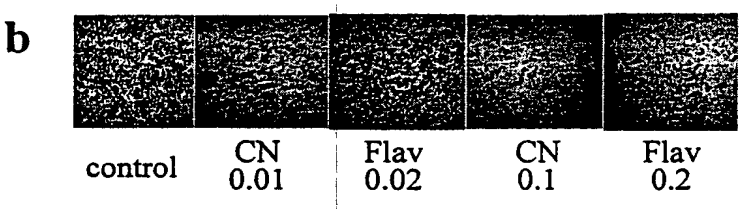

b
control
CN 0.01
Flav 0.02
CN 0.1
Flav 0.2

FIG. 10

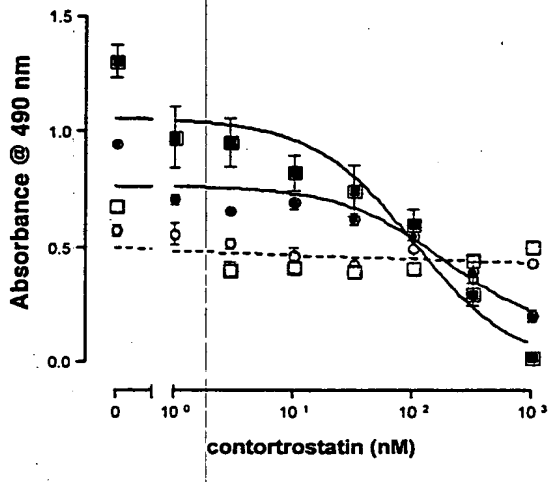

Absorbance @ 490 nm
1.5
1.0
0.5
0.0
0
10 0
10 1
10 2
10 3
contortrostatin (nM)

FIG. 11

FIG. 12

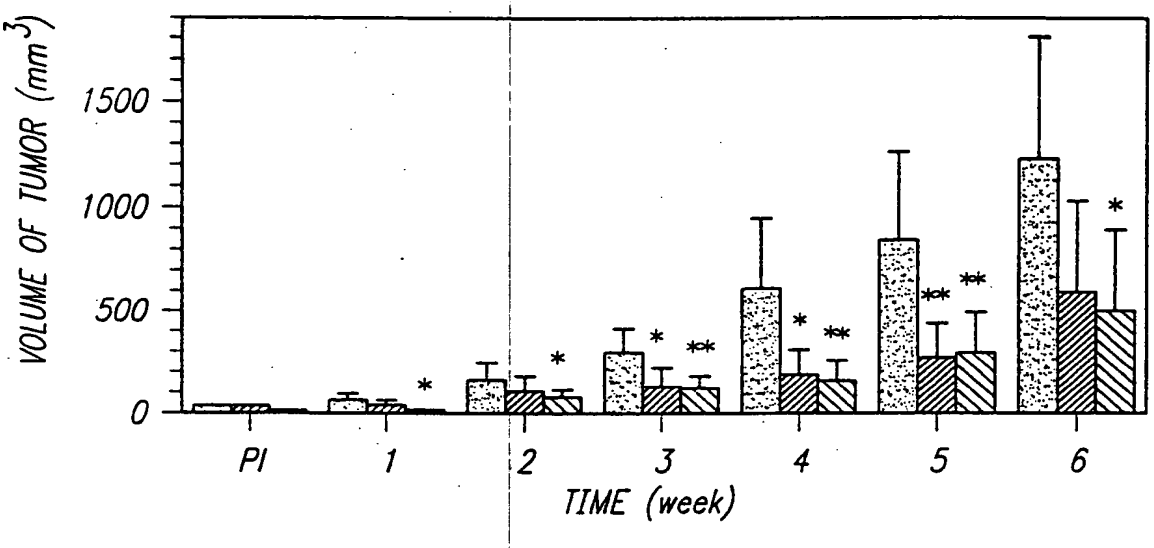
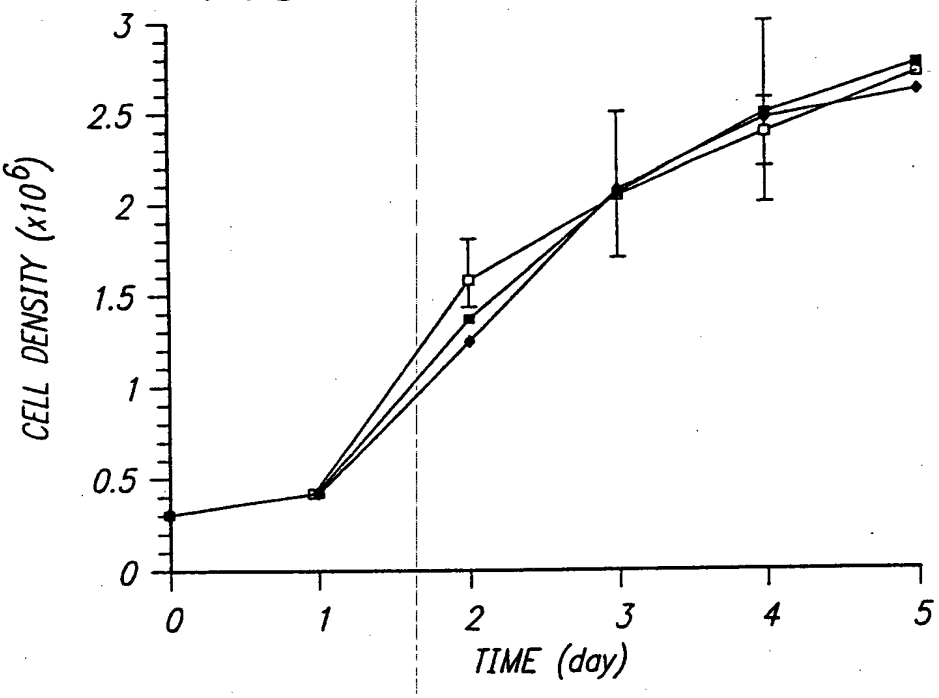


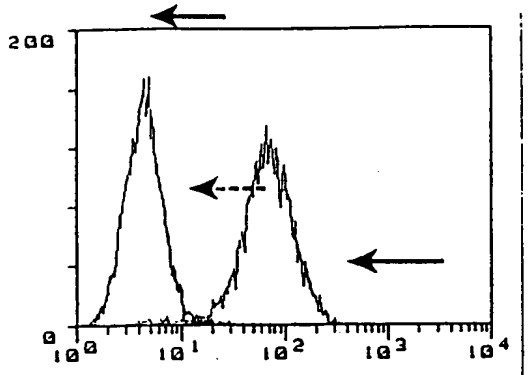
FIG. 13A

FIG. 13B

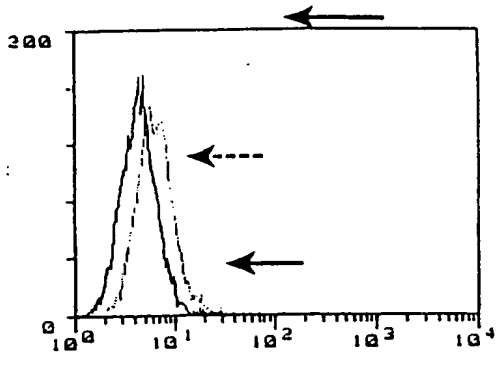
FIG. 13C

FIG. 14

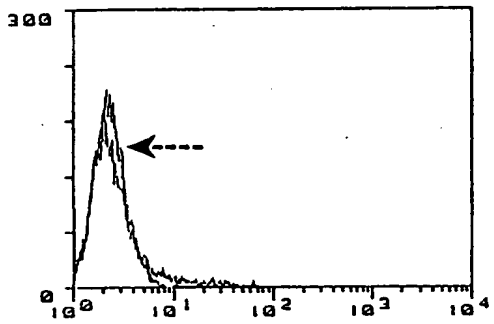



200
0
10^0
10^1
10^2
10^3
10^4

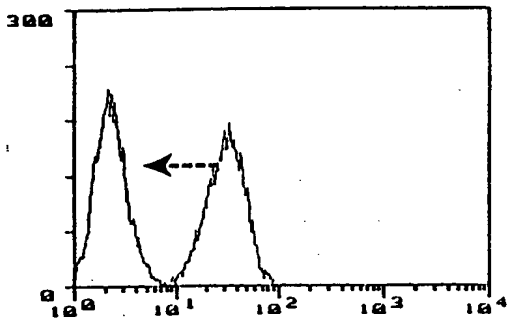
(A)


200
0
10^0
10^1
10^2
10^3
10^4

(B)


300
0
10^0
10^1
10^2
10^3
10^4

(C)


300
0
10^0
10^1
10^2
10^3
10^4

(D)

FIG. 15

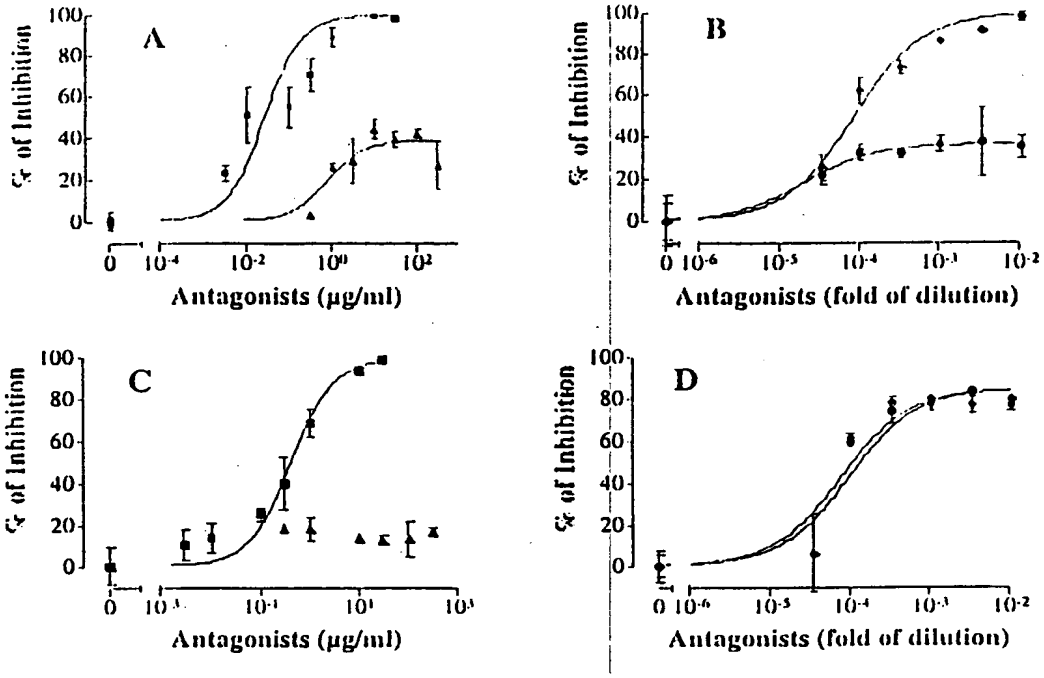

A
B
C
D
% of Inhibition
Antagonists (μg/ml)
Antagonists (fold of dilution)

FIG. 16

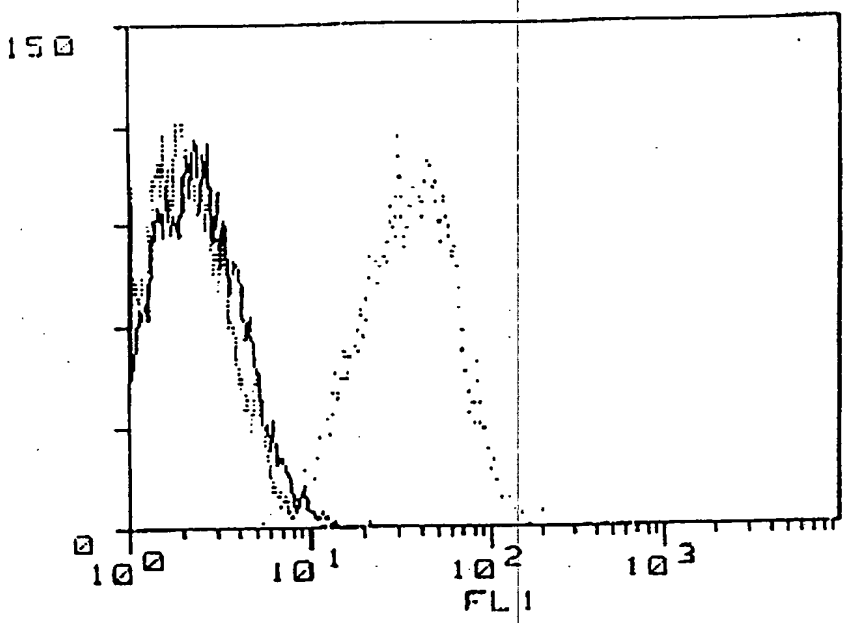


FIG. 17

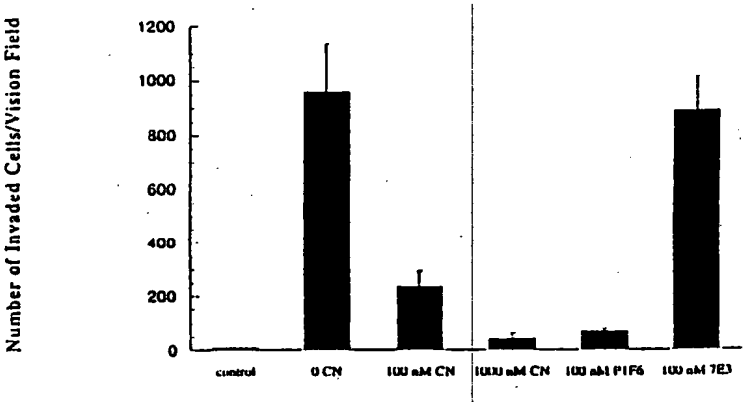

Number of Invaded Cells/Vision Field
1200
1000
800
600
400
200
0
control
0 CN
100 aM CN
1000 aM CN
100 aM P1F6
100 aM 7E3

FIG. 18

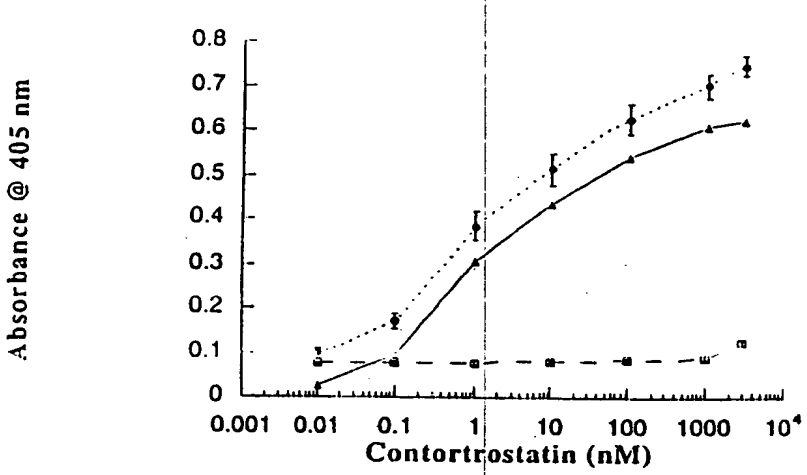

Absorbance @ 405 nm
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.001
0.01
0.1
1
10
100
1000
10^4
Contortrostatin (nM)

FIG. 19

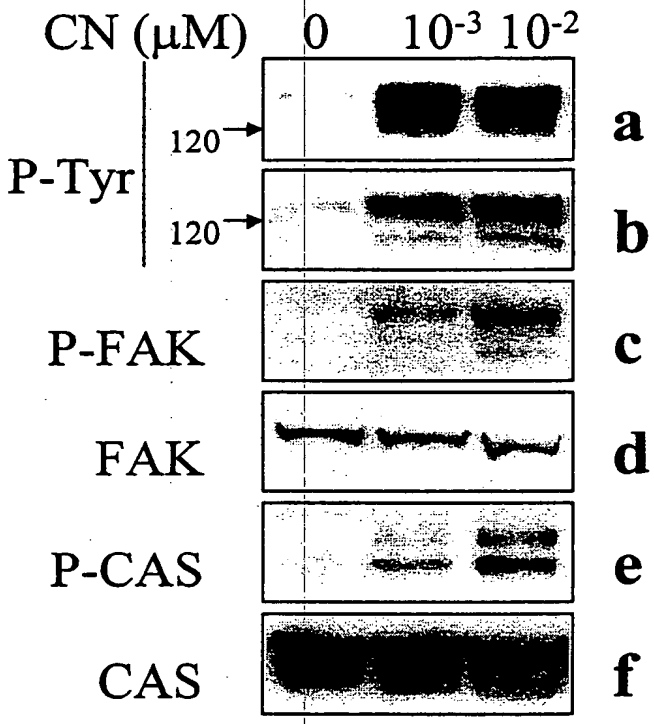


FIG. 20

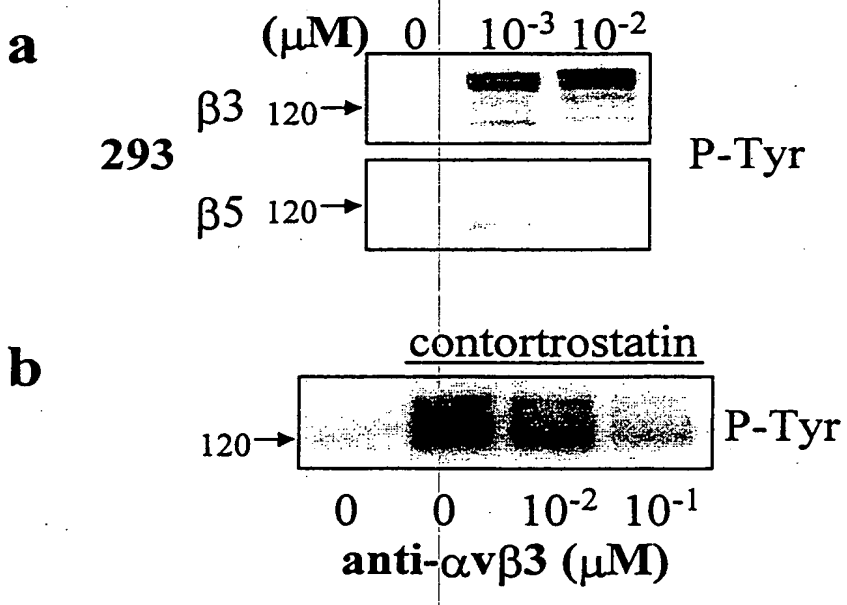

a
(μM) 0 10-3 10-2
β3 120→
293
P-Tyr
β5 120→
b
contortrostatin
120→
P-Tyr
0 0 10-2 10-1
anti-αvβ3 (μM)

FIG. 21

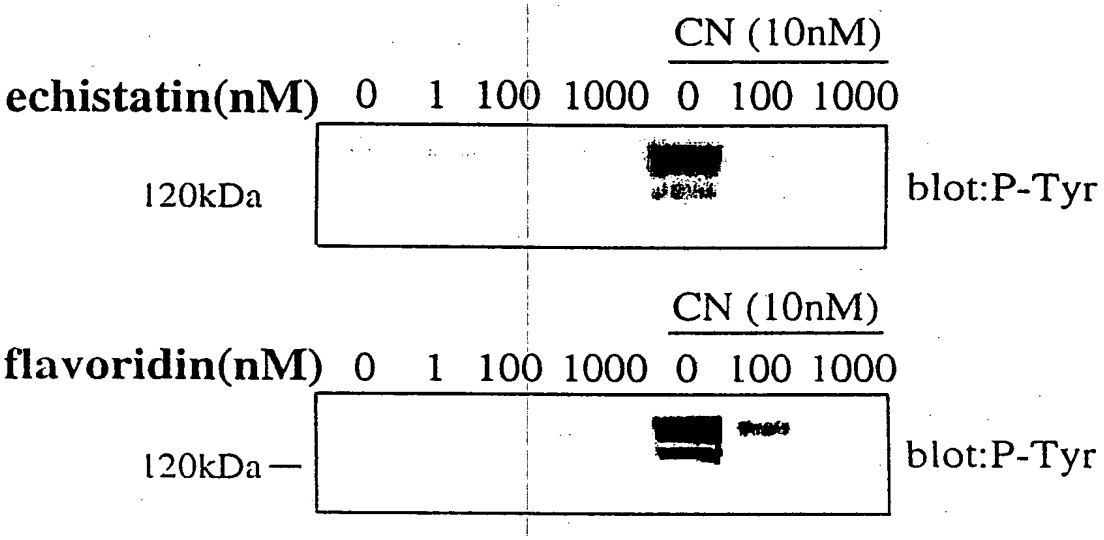
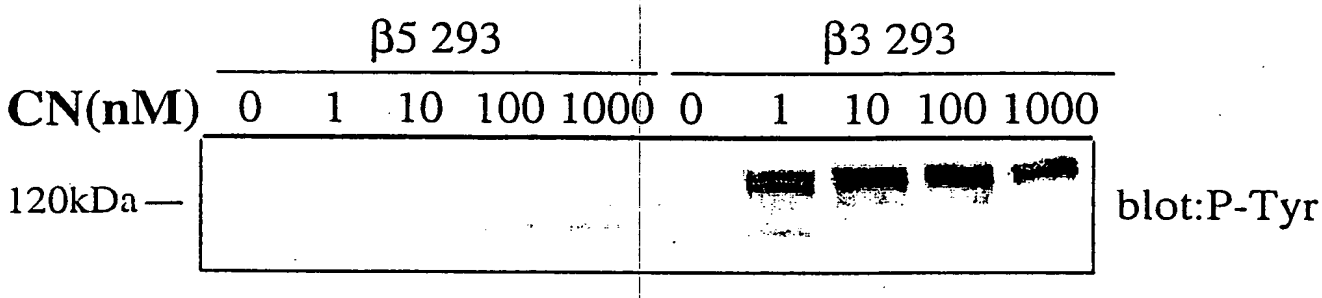
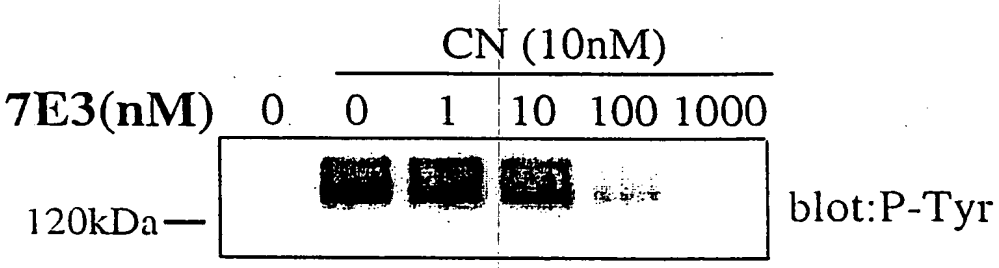

CN (10nM)
echistatin(nM) 0 1 100 1000 0 100 1000
120kDa
blot:P-Tyr
CN (10nM)
flavoridin(nM) 0 1 100 1000 0 100 1000
120kDa
blot:P-Tyr

FIG. 22

A


β5 293
β3 293
CN(nM) 0 1 10 100 1000 0 1 10 100 1000
120kDa—
blot:P-Tyr

B


CN (10nM)
7E3(nM) 0 0 1 10 100 1000
120kDa—
blot:P-Tyr

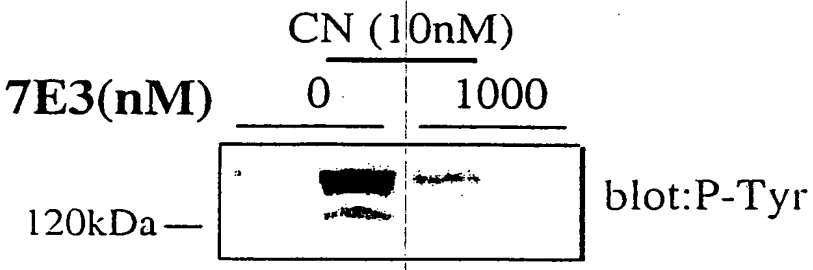

CN (10nM)
7E3(nM) 0 1000
120kDa—
blot:P-Tyr

FIG. 23

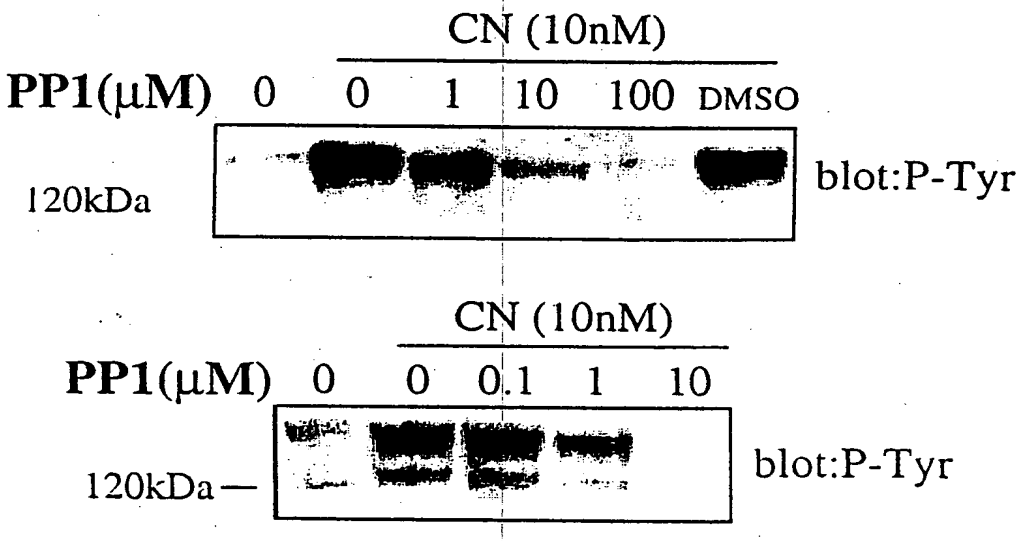

CN (10nM)
PP1(μM) 0 0 1 10 100 DMSO
120kDa
blot:P-Tyr
CN (10nM)
PP1(μM) 0 0 0.1 1 10
120kDa
blot:P-Tyr

FIG. 24

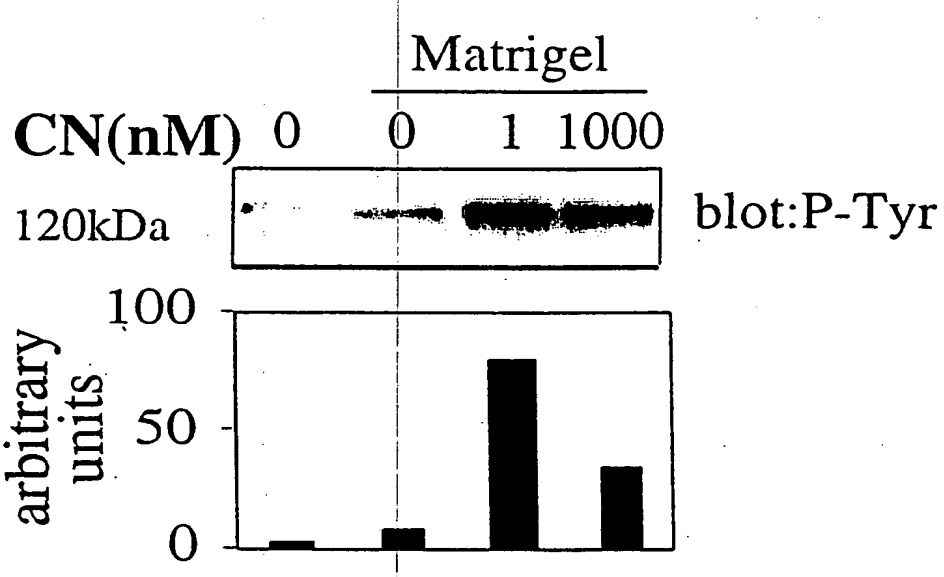

Matrigel
CN(nM) 0 0 1 1000
120kDa
blot:P-Tyr
100
50
0
arbitrary units

FIG. 25

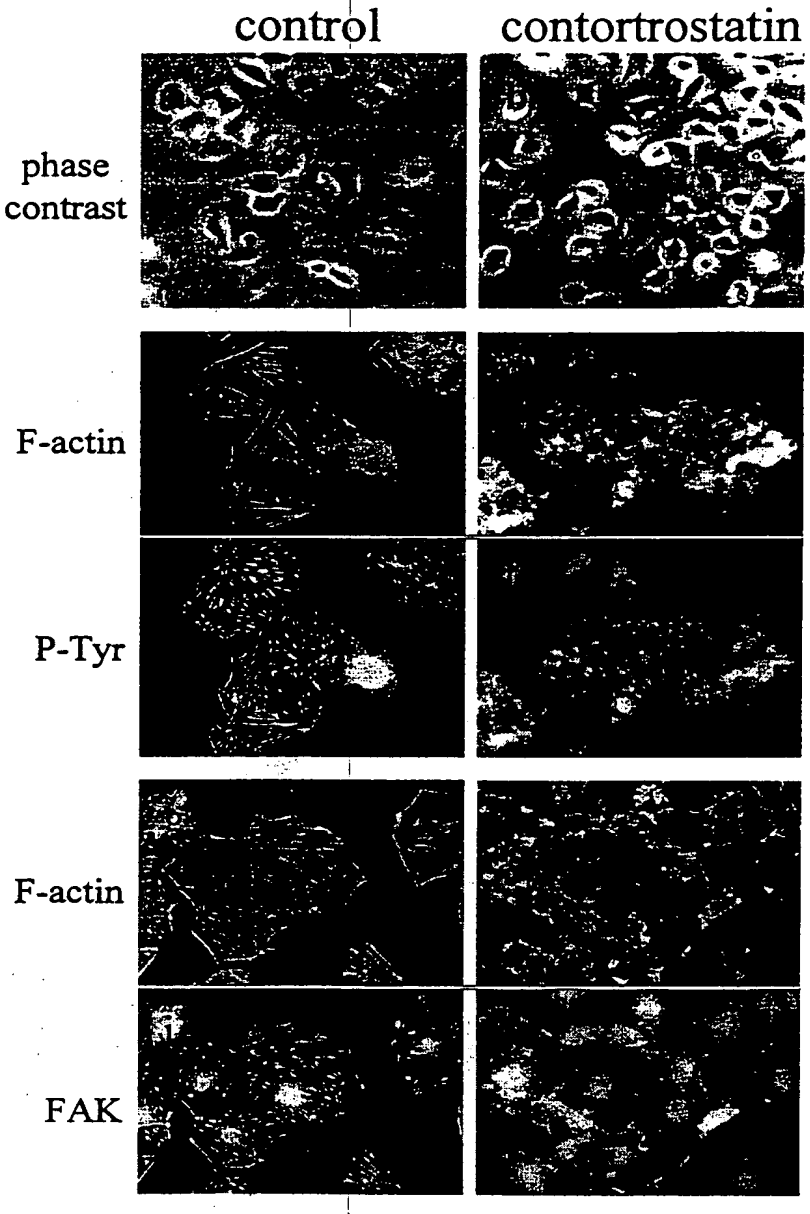

control
contortrostatin
phase contrast
F-actin
P-Tyr
F-actin
FAK

FIG. 26

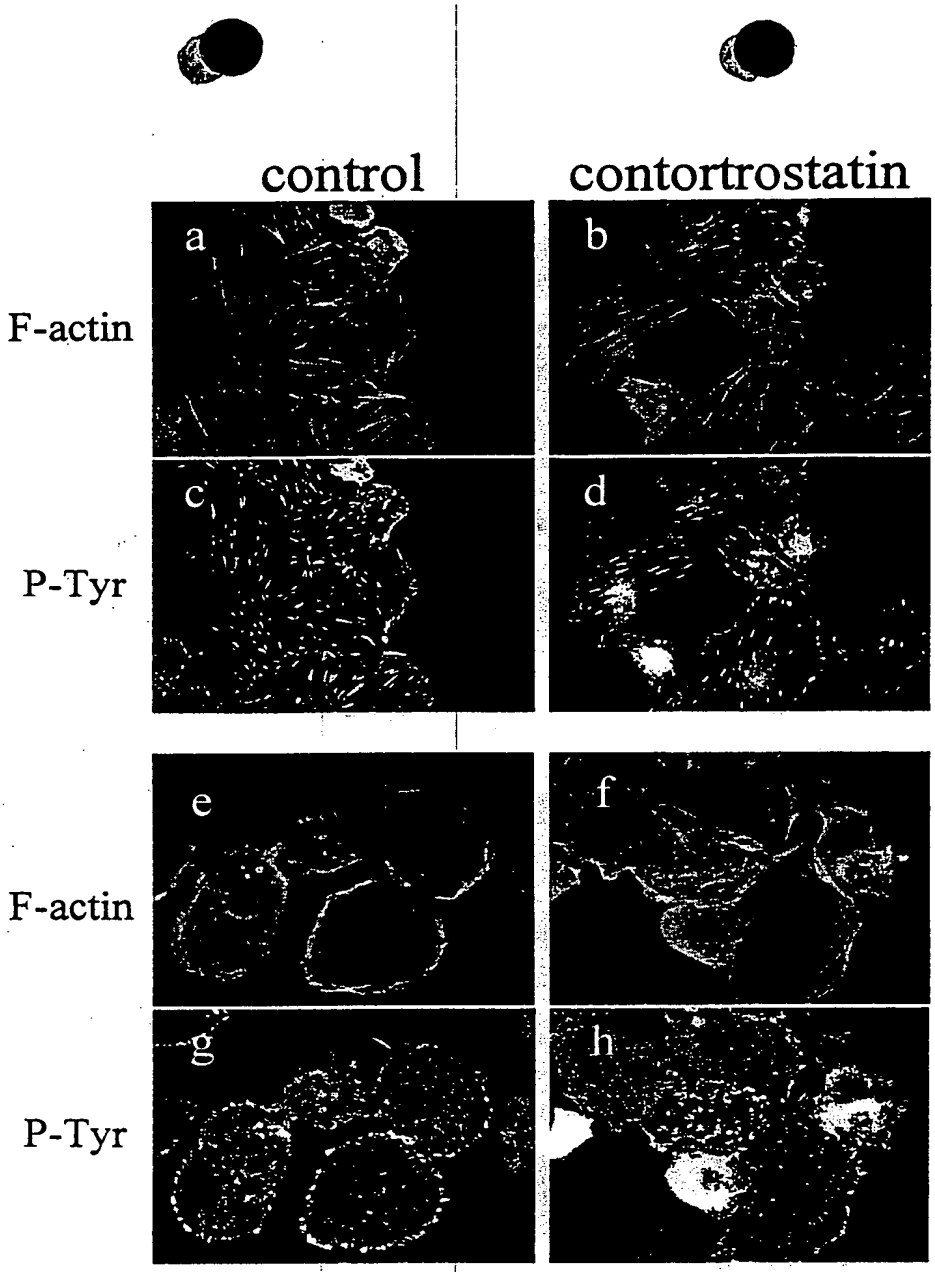

control
contortrostatin
a
b
F-actin
c
d
P-Tyr
e
f
F-actin
g
h
P-Tyr

FIG. 27

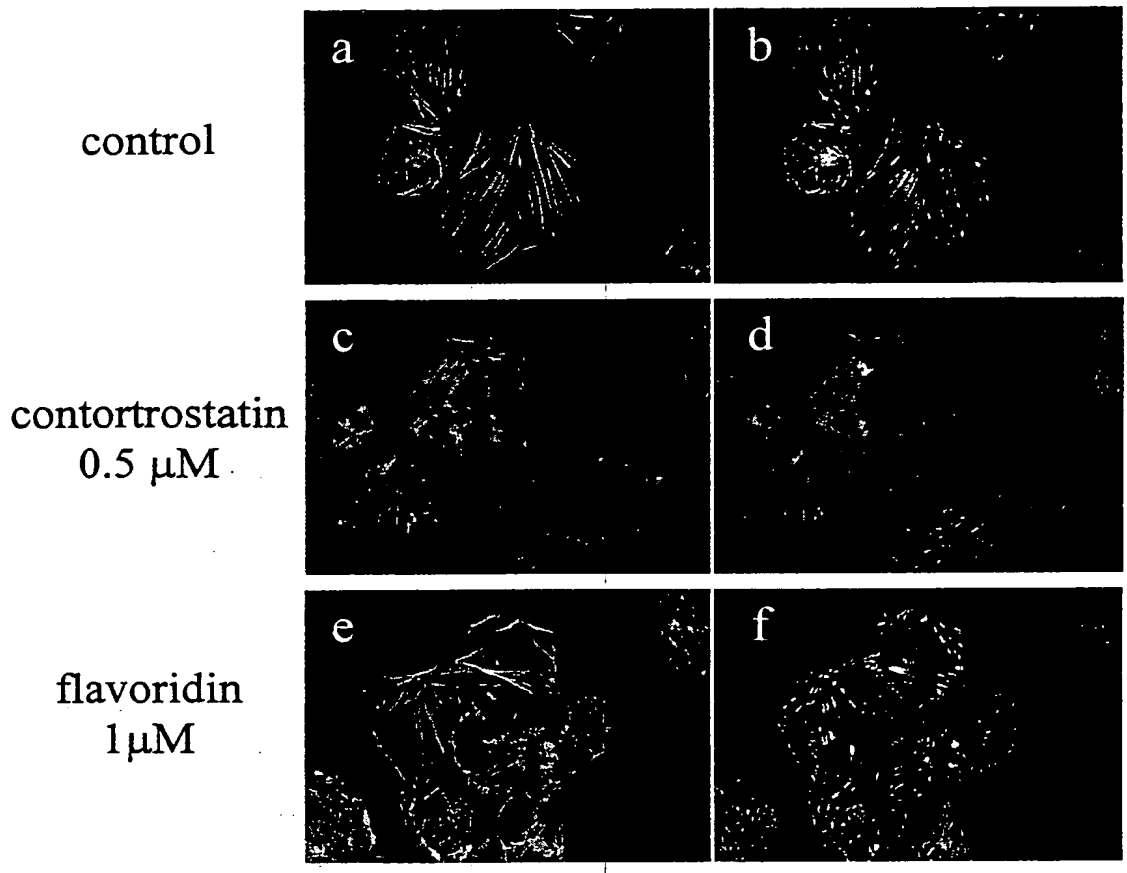

F-actin
P-Tyr
a
b
control
c
d
contortrostatin
0.5 μM
e
f
flavoridin
1μM

FIG. 28

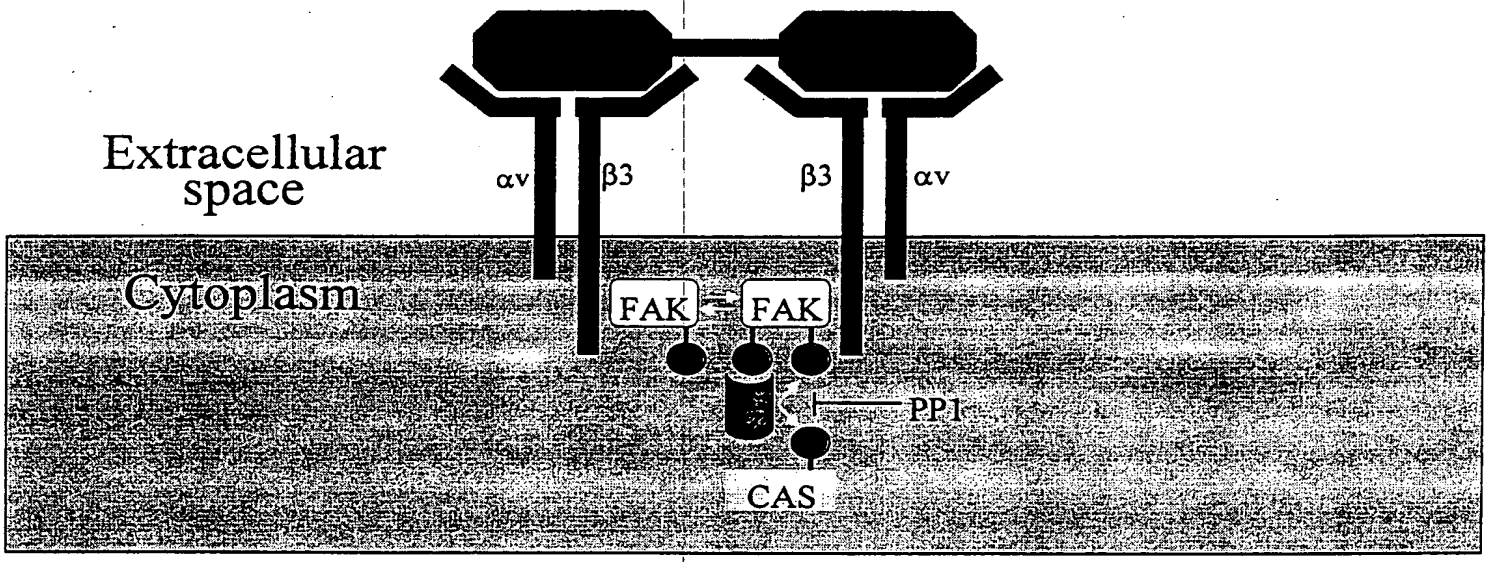


FIG. 29

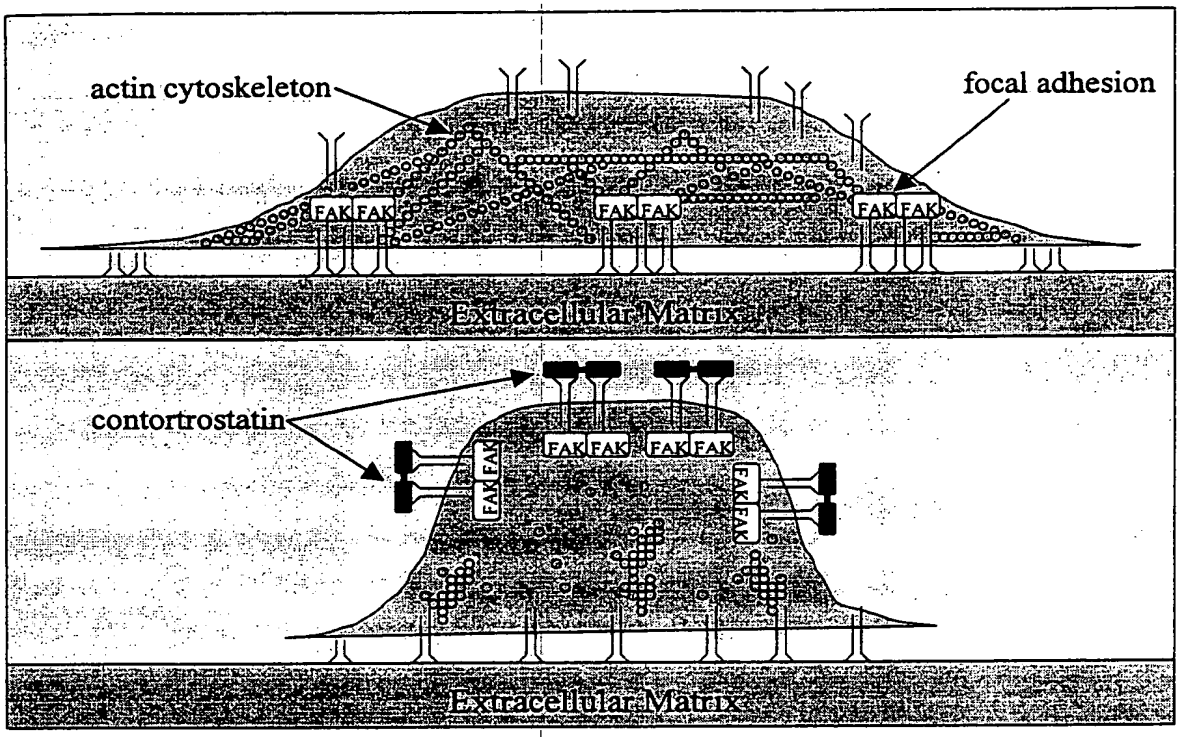

actin cytoskeleton
focal adhesion
FAK
Extracellular Matrix
contortrostatin
Extracellular Matrix

FIG. 30